

# CORRESPONDENCE

## Vaccination Safety Update

by Prof. Dr. med. habil. Burkhard Schneeweiß, Dr. rer. nat. Michael Pfeiderer, Dr. med. Brigitte Keller-Stanislawski in volume 34–35/2008

### Macrophagic Myofasciitis

We wish to raise awareness of the phenomenon of macrophagic myofasciitis (MMF), which does exist in Germany but has not received much attention. This phenomenon may develop after vaccination. MMF is an acquired inflammatory muscular lesion that manifests focally as round cells located in the perifascicular space while the remaining muscle fibers remain relatively intact. Histopathologically, MMF is characterized by macrophages that are positive for diastase resistant periodic acid-Schiff (PAS) and numerous CD8+ T cells. Tissue necrosis or giant cells are typically not detected. As an expression of lysosomal activity, the macrophages are strongly positive for "acidic phosphatase" and "nonspecific esterase". Electron microscopic studies regularly show numerous needle-shaped structures within the lysosomes of these macrophages. By analyzing a tissue section—so called laser microprobe mass analysis (LAMMA)—the needle-shaped structures can be identified as aluminum hydroxide.

In adults it is almost exclusively the left deltoid muscle ('vaccination muscle') that is affected, in children almost exclusively the quadriceps.

Different working groups, mainly in France, postulate a causal association between MMF, aluminium hydroxide containing vaccines—for example, the hepatitis B, hepatitis A, tetanus toxoid vaccines and systemic clinical symptoms. The clinical spectrum, which may occur even up to 10 years after the vaccination, is unspecific and ranges from myalgias and arthralgias to increased fatigue (1, 2).

A comprehensive epidemiological follow-up to establish a possible causal association between focal MMF lesions after vaccination, the use of aluminium hydroxide, and systemic clinical symptoms is required—which, as far as we know, has not been undertaken so far. However—and this is an important message—it is absolutely in no way our intention to question the need for the mentioned vaccinations. DOI: 10.3238/arztebl.2009.0248a

Illustrations on the topic available from the authors.

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### Conflict of interest statement

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### Long Term Side Effects Due to Vaccination And Pharmacovigilance

We thank the authors for their clear overview of vaccine sceptics' common objections, which are helpful for everyday clinical practice.

Most vaccinations and vaccination advice in Germany are given by general practitioners and pediatricians. Appropriate and responsible advice includes providing information to those about to receive the vaccine and their parents, about rare but possible side effects. These include the possible occurrence of Guillain-Barré syndromes after flu vaccinations (1), for example; the possible association between recombinant hepatitis B vaccine and multiple sclerosis (2), which is still under discussion in current publications; and the unexplained possible association of multiple vaccinations with neurodegenerative disorders in connection with aluminum hydroxide, which to date is the most common vaccine adjuvant in use (3).

Long term side effects due to vaccination can be detected to a sufficiently high quality standard only by means of long term, active pharmacovigilance conducted through independent and sufficiently equipped monitoring systems. To assess the long term safety of vaccines, passive post-vaccination observation by notification of vaccination complications by primary care physicians is not enough: possible causal associations with developing disorders—for example, neurodegenerative disorders—are difficult to state in individual cases years after the vaccine was given. DOI: 10.3238/arztebl.2009.0248b

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### In Reply:

Higher demands are made on the safety of vaccines than on medication used to treat serious disorders, because vaccines are usually used in healthy persons. We therefore wholeheartedly support Dr Klement's demand for well equipped and efficient monitoring systems in the interest of drug safety. Even in comprehensively tested vaccines it cannot be ruled out that very rare side effects will be observed for the first time once a vaccine has started to be widely used. It is therefore necessary to identify signs of possible side effects speedily and to investigate them reliably.

Of importance in this context are not only national efforts to improve pharmacovigilance but also cooperation among the EU authorities. A good example is the EudraVigilance database of the European Medicines Agency (EMA; [www.europa.emea.eu](http://www.europa.emea.eu)). This contains one of the biggest side effect databases worldwide and is accessible for national authorities. The recently published EMA recommendation, the "Guideline on the Conduct of Pharmacovigilance for Vaccines for Pre- and Post-exposure Prophylaxis against Infectious Diseases"

(<http://www.emea.europa.eu/pdfs/human/phvwp/50344907en.pdf>), for example, describes the requirements for pharmacovigilance of vaccines in the EU. Diverse WHO initiatives are also worth mentioning—such as the Global Advisory Committee on Vaccine Safety (GACVS; [http://www.who.int/vaccine\\_safety/en/](http://www.who.int/vaccine_safety/en/)), which publishes evidence based assessments regarding perceived vaccination risks, and the attempts by the WHO/CIOMS working group to standardize pharmacovigilance of vaccines ([http://www.cioms.ch/jan2008\\_current\\_programme\\_and\\_planned\\_activities.pdf](http://www.cioms.ch/jan2008_current_programme_and_planned_activities.pdf)).

Macrophagic fasciitis, as mentioned by Dr Stenzel and colleagues, is one of the rare vaccination signs whose importance for systemic health impairment is unclear. In our limited overview we were able to discuss neither this, nor several other hypotheses, but we are in the process of preparing a separate publication on the subject.

One of the main objectives of our review article was to emphasize the need for doctors to notify any suspected vaccination related complication—this is central to pharmacovigilance. To detect signs early on, it is desirable that health impairments are also notified that may occur owing to a temporal, but possible not causal, association with the vaccination.

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